CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and at least two recombinant rabies virus-neutralizing human antibodies, wherein at least one of the at least two antibodies is selected from the group consisting of:

a) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:2 or a sequence that is substantially homologous to SEQ ID NO:2, and an antibody heavy chain having the amino acid sequence SEQ ID NO:1 or a sequence that is substantially homologous to SEQ ID NO:1;

b) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:6 or a sequence that is substantially homologous to SEQ ID NO:6, and an antibody heavy chain having the amino acid sequence SEQ ID NO:4 or a sequence that is substantially homologous to SEQ ID NO:4; and

c) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:7 or a sequence that is substantially homologous to SEQ ID NO:7, and an antibody heavy chain having the amino acid sequence SEQ ID NO:9 or a sequence that is substantially homologous to SEQ ID NO:9.

2. The pharmaceutical composition of claim 1, comprising:

a) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:2 or a sequence that is substantially homologous to SEQ ID NO:2, and an antibody heavy chain having the amino acid sequence SEQ ID NO:1 or a sequence that is substantially homologous to SEQ ID NO:1;

b) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:6 or a sequence that is substantially homologous to SEQ ID NO:6, and an antibody heavy chain having the amino acid sequence SEQ ID NO:4 or a sequence that is substantially homologous to SEQ ID NO:4; and

c) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:7 or a sequence that is substantially homologous to SEQ ID NO:7, and an antibody heavy chain having the amino acid sequence SEQ ID NO:9 or a sequence that is substantially homologous to SEQ ID NO:9.

3. The pharmaceutical composition of claim 2, comprising:

a) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:2 and an antibody heavy chain having the amino acid sequence SEQ ID NO:1;

b) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:6 and an antibody heavy chain having the amino acid sequence SEQ ID NO:4; and

c) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:7 and an antibody heavy chain having the amino acid sequence SEQ ID NO:9.

4. A method of treating or preventing a rabies virus infection in a subject in need of such treatment, comprising administering to the subject an effective amount of at least two recombinant rabies virus-neutralizing human antibodies, wherein at least one of the at least two antibodies is selected from the group consisting of:

a) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:2 or a sequence that is substantially homologous to SEQ ID NO:2, and an antibody heavy chain having the amino acid sequence SEQ ID NO:1 or a sequence that is substantially homologous to SEQ ID NO:1;

b) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:6 or a sequence that is substantially homologous to SEQ ID NO:6, and an antibody heavy chain having the amino acid sequence SEQ ID NO:4 or a sequence that is substantially homologous to SEQ ID NO:4; and

c) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:7 or a sequence that is substantially homologous to SEQ

ID NO:7, and an antibody heavy chain having the amino acid sequence SEQ ID NO:9 or a sequence that is substantially homologous to SEQ ID NO:9.

5. The method of claim 4, wherein the at least two recombinant rabies virus-neutralizing human antibodies exhibit neutralizing activity against different rabies viruses.

6. The method of claim 5, wherein the at least two different recombinant rabies virus-neutralizing human antibodies are separately administered.

7. The method of claim 5, wherein at least three different recombinant rabies virus-neutralizing human antibodies are administered.

8. The method of claim 4, wherein the recombinant rabies virus-neutralizing human antibodies comprise:

a) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:2 or a sequence that is substantially homologous to SEQ ID NO:2, and an antibody heavy chain having the amino acid sequence SEQ ID NO:1 or a sequence that is substantially homologous to SEQ ID NO:1;

b) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:6 or a sequence that is substantially homologous to SEQ ID NO:6, and an antibody heavy chain having the amino acid sequence SEQ ID NO:4 or a sequence that is substantially homologous to SEQ ID NO:4; and

c) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:7 or a sequence that is substantially homologous to SEQ ID NO:7, and an antibody heavy chain having the amino acid sequence SEQ ID NO:9 or a sequence that is substantially homologous to SEQ ID NO:9.

9. The method of claim 8, wherein the recombinant rabies virus-neutralizing human antibodies comprise:

a) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:2 and an antibody heavy chain having the amino acid sequence SEQ ID NO:1;

b) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:6 and an antibody heavy chain having the amino acid sequence SEQ ID NO:4; and

c) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:7 and an antibody heavy chain having the amino acid sequence SEQ ID NO:9.

10. The method of claim 5, wherein the recombinant rabies virus-neutralizing human antibodies are administered in a mixture of approximately equimolar concentrations.

11. The method of claim 5, wherein the recombinant rabies virus-neutralizing human antibodies are administered in approximately equal amounts by weight.

12. The method of claim 11, wherein the amount of antibody administered is between about 0.001 mg/kg body weight and about 100 mg/kg body weight.

13. The method of claim 12, wherein the amount of antibody administered is between about 0.01 mg/kg body weight and about 60 mg/kg body weight.

14. The method of claim 5, wherein the at least three different recombinant rabies virus-neutralizing human antibodies comprise between about 1 IU/kg body weight and about 50 IU/kg body weight rabies virus-neutralizing activity.

15. The method of claim 5, wherein the rabies virus is a fixed rabies virus or a street rabies virus.

16. The method of claim 15, wherein the street rabies virus is selected from the group consisting of silver-haired bat rabies virus, coyote street rabies virus/Mexican dog rabies virus, and dog rabies virus.

17. The method of claim 16, wherein the silver-haired bat rabies virus is silver-haired bat rabies virus-18.

18. The method of claim 16, wherein the dog rabies virus is dog rabies virus-4.

19. The method of claim 5, wherein the subject is a human.

20. The method of claim 5, wherein the at least two recombinant rabies virus-neutralizing human antibodies are administered parenterally.

21. The method of claim 20, wherein the parenteral administration is selected from the group consisting of intravascular administration, peri- and intra-tissue injection, intraperitoneal injection, subcutaneous injection, subcutaneous deposition, and subcutaneous infusion.

22. A recombinant rhabdovirus expression vector, comprising: (i) a nucleic acid sequence encoding a vesicularstomatitisvirus glycoprotein sequence; and (ii) a nucleic acid sequence encoding an antibody light chain, or an antibody heavy chain, or both an antibody light chain and an antibody heavy chain, of a recombinant rabies virus-neutralizing human antibody.

23. The recombinant rhabdovirus expression vector of claim 22, wherein the vector further comprises a nucleic acid sequence encoding a promoter sequence operably linked to the (i) the nucleic acid sequence encoding

a vesicularstomatitisvirus glycoprotein sequence; and (ii) the nucleic acid sequence encoding an antibody light chain, or an antibody heavy chain, or both an antibody light chain and an antibody heavy chain, of a recombinant rabies virus-neutralizing human antibody.

24. The recombinant rhabdovirus expression vector of claim 23, wherein the vector encodes an antibody light chain selected from the group consisting of:

a) an antibody light chain having the amino acid sequence SEQ ID NO:2 or a sequence that is substantially homologous to SEQ ID NO:2;

b) an antibody light chain having the amino acid sequence SEQ ID NO:6 or a sequence that is substantially homologous to SEQ ID NO:6; and

c) an antibody light chain having the amino acid sequence SEQ ID NO:7 or a sequence that is substantially homologous to SEQ ID NO:7.

25. The recombinant rhabdovirus expression vector of claim 23, wherein the vector encodes an antibody heavy chain selected from the group consisting of:

a) an antibody heavy chain having the amino acid sequence SEQ ID NO:1 or a sequence that is substantially homologous to SEQ ID NO:1;

b) an antibody heavy chain having the amino acid sequence SEQ ID NO:4 or a sequence that is substantially homologous to SEQ ID NO:4; and

c) an antibody heavy chain having the amino acid sequence SEQ ID NO:9 or a sequence that is substantially homologous to SEQ ID NO:9.

26. A host mammalian cell comprising a recombinant rhabdovirus expression vector selected from the group consisting of the recombinant rhabdovirus expression vectors according to claims 22, 23, 24, and 25.

27. The host mammalian cell of claim 26, wherein the mammalian cell is selected from the group consisting of BSR cells, baby hamster cells, VERO cells, and chinese hamster ovary cells.

28. A method of producing a recombinant rabies virus-neutralizing human antibody in a mammalian cell, comprising culturing a cell of claim 26, under conditions which allow expression of the recombinant rabies virus-neutralizing human antibody.

29. The method of claim 28, wherein the recombinant rabies virus-neutralizing human antibody is produced in a mammalian cell selected from the group consisting of BSR cells, baby hamster cells, VERO cells, and chinese hamster ovary cells.

30. Use of a combination of at least two recombinant rabies virus-neutralizing human antibodies, wherein at least one of the antibodies is selected from the group consisting of:

a) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:2 or a sequence that is substantially homologous to SEQ ID NO:2, and an antibody heavy chain having the amino acid sequence SEQ ID NO:1 or a sequence that is substantially homologous to SEQ ID NO:1;

b) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:6 or a sequence that is substantially homologous to SEQ ID NO:6, and an antibody heavy chain having the amino acid sequence SEQ ID NO:4 or a sequence that is substantially homologous to SEQ ID NO:4; and

c) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:7 or a sequence that is substantially homologous to SEQ ID NO:7, and an antibody heavy chain having the amino acid sequence SEQ ID NO:9 or a sequence that is substantially homologous to SEQ ID NO:9;

for preparation of a medicament for treating or preventing a rabies virus infection in a subject in need of such treatment.

31. Use of a combination according to claim 30, wherein the at least two recombinant rabies virus-neutralizing human antibodies exhibit neutralizing activity against different rabies viruses.

32. Use of a combination of antibodies according to claim 30, wherein the combination comprises at least three different recombinant rabies virus-neutralizing antibodies.

33. Use of a combination of antibodies according to claim 32, wherein the antibodies comprise:

a) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:2 or a sequence that is substantially homologous to SEQ ID NO:2, and an antibody heavy chain having the amino acid sequence SEQ ID NO:1 or a sequence that is substantially homologous to SEQ ID NO:1;

b) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:6 or a sequence that is substantially homologous to SEQ ID NO:6, and an antibody heavy chain having the amino acid sequence SEQ ID NO:4 or a sequence that is substantially homologous to SEQ ID NO:4; and

c) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:7 or a sequence that is substantially homologous to SEQ ID NO:7, and an antibody heavy chain having the amino acid sequence SEQ ID NO:9 or a sequence that is substantially homologous to SEQ ID NO:9.

34. Use of a combination of antibodies according to claim 33, wherein the antibodies comprise:

a) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:2 and an antibody heavy chain having the amino acid sequence SEQ ID NO:1;

b) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:6 and an antibody heavy chain having the amino acid sequence SEQ ID NO:4; and

c) an antibody comprising an antibody light chain having the amino acid sequence SEQ ID NO:7 and an antibody heavy chain having the amino acid sequence SEQ ID NO:9.